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Anticholinergic Responsive Cyclic Myoclonus

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Episodic neurological disorders with a fixed interval are rare. Previously, we described a case of anticholinergic responsive cyclic oculogyric crisis.¹ Here, we report on another case of anticholinergic responsive cyclic movement disorders.

This 84-year-old right-handed woman has been bed-ridden for the past 30 years after a hip fracture and also has a long history of chin/tongue/lip tremor and hand rest tremor. She took quetiapine (25 mg) at bedtime for insomnia for several weeks and developed cyclic myoclonus every 3 days for 6 months. During the episode, she had whole-body myoclonus with some components of dystonia, jaw-opening dystonia, and autonomic symptoms, including fever (up to 101°F), tachycardia (up to 126/min), and tachypnea (up to 24/min), which lasted 16 to 24 hours. Her consciousness was preserved during the event. Myoclonus was involuntary and multifocal, involving her neck, trunk, and four extremities, and occurred at rest or in action (see Video, Segment 1). After the episode, she fell asleep for approximately 48 hours in various stages of sleep confirmed by EEG. This cycle repeated itself every 3 days. She had no eye-movement abnormalities, but mild rigidity, bradykinesia, and rest tremor between episodes. Quetiapine was stopped, but cyclic myoclonus persisted. MRI of the brain showed biparietal sulcal atrophy and moderate ventricular dilatation. EEG during the event showed no evidence of epileptiform discharges. Cerebrospinal fluid analysis showed normal protein and glucose without white blood cells. Paraneoplastic and paninfectious work-up were unremarkable. [¹⁸F]-fluorodeoxyglucose PET revealed decreased metabolism in the bilateral frontal and parietotemporal lobes, consistent with the frontal variant of Alzheimer's disease.

She was treated with levodopa (up to 300 mg/day) for 1 month or levetiracetam (1,000 mg twice-daily; BID) for 2 weeks, which did not eliminate myoclonus. Bromocriptine (2.5 mg BID) made her hypersomnolent, and she required a percutaneous endoscopic gastrostomy (PEG) tube to supply her nutrition. Because of the previous experience with the case with cyclic oculogyric crisis,¹ we used benztropine (1.25 mg BID), which effectively aborted her

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cyclic episodes (see Video, Segment 2). Her chin/tongue/lip tremor also largely resolved. She still had occasional myoclonus in her hands without the cyclic episodes. Her swallowing function improved, and the PEG tube was removed. She has remained event free on the regimen for at least 1.5 years, and benztropine was well tolerated and did not worsen her cognition.

Episodic neurological disorders are usually associated with neuronal channelopathies²; however, intervals between episodes are usually variable. In this case, recurrent myoclonic status epilepticus could be the differential diagnosis, but the fixed intervals between the episodes without definite epileptiform activities on EEG and the lack of response to levetiracetam make these episodes unlikely to be epileptic. Recurrent seizures with fixed intervals have been reported on in critically ill patients, and, usually, intervals are several hours and each event only lasts for minutes.³ In this case, we are not certain about the etiology of the cyclic myoclonus. It could be related to history of quetiapine use or underlying neurodegenerative processes. The myoclonus could be cortical in origin, given its multifocal nature.

The lack of good response of her parkinsonism to dopaminergic agents suggests that cyclic myoclonus is not purely a presynaptic dopaminergic deficiency state. Postsynaptic structure, such as striatum, could be involved. The dramatic response to benztropine indicates a role of the cholinergic system in cyclic myoclonus. Cholinergic interneurons comprised approximately 5% of striatal cell populations and have an important role in modulating striatal physiology,⁴ and the imbalance of cholinergic and dopaminergic transmission systems could contribute to cyclic myoclonus with parkinsonism. In fact, earlier studies have shown that the cholinergic system could play a role in myoclonus.^{5,6} Disturbance of circadian rhythm also implies that the reticular activating system could also be involved in this case.

We did not withdraw benztropine, so as to clearly demonstrate the effectiveness of the medicine. Nonetheless, we believe that reporting on such a rare case would be beneficial to movement disorder clinicians, who should consider anticholinergics to treat cyclic movement disorders.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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